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EXAMINER	
KWON, BRIAN YONG S	

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/053,962	GIBSON, KAREN	
	Examiner	Art Unit	
	Brian S Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/5/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

1. Applicant's arguments with respect to claims 1-42 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 39-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 39-42 provide for the use of devazepide, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

3. Claims 21-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The dependent claims 21-22 further limit the subject matter of claims 1 and 2 by reciting the specific dosage amounts of devazepide, specifically "up to 0.7 mg/kg/day". Since the interpretation of "up to 0.7mg/kg/day" includes the possibility of having no devazepide (if the lower range of devazepide is 0.0mg/kg/day) in the claimed method, the claims leave the reader in

doubt as to the meaning of the invention to which they refer, thereby rendering the definition of the subject-matter of said claims unclear.

Claim Rejections - 35 USC § 101

4. Claims 39-42 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-14, 19-26, 29-30, 43 and 45 are rejected under 35 U.S.C. 102(b) as being anticipated by Dourish et al. (The Journal of Pharmacology And Experimental Therapeutics, Vol. 255, No. 3, 1990, pp. 1158-65).

Dourish expressly teaches use of devazepide which is a selective CCK-A antagonist as an adjuvant to morphine (i.e., morphine HCl) analgesic allowing lower doses of the opiate to be used to relieve pain and reducing the risk of opiate-induced respiratory depression (abstract; page 1163, column 2, para. 3 thru page 1164, column 1, para. 1). Dourish discloses the instantly

required administration of the devazepide and/or the opioid in various dosage forms (i.e., p.o., i.p., i.v., s.c.) and overlapping dosage amounts of devazepide, for example 1, 3, 10, 30, 100 and 300 μg/kg (see Methods and Results).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. Claims 15-18, 27-28, 31-38, 44 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dourish et al. (The Journal of Pharmacology And Experimental Therapeutics, Vol. 255, No. 3, 1990, pp. 1158-65), and if necessary further in view of Loh et al. (US 4361553) and Gardocki et al. (US 4338324).

The teaching of Dourish has been discussed in above 35 USC 102(b) rejection. In addition, Dourish discloses that the clinical utility of morphine as an analgesic is limited by a

number of undesirable side effects including nauseas, emesis, constipation and respiratory depression (page 1990, column 1, first three lines of para. 3).

It is noted to applicant that Loh and Gardocki are being supplied as references to demonstrate "a continuing search for a combination of two or more drugs whereby the total quantity of drug can be reduced and which can be employed in such proportions as to produce maximum analgesic effect with little or no side effects" as a routine knowledge in the art. Furthermore, Loh and Gardocki are being supplied as references to demonstrate "morphine, morphine salts (such as morphine hydrobromide, morphine hydrochloride, morphine mucate, morphine oleate, morphine N-oxide and morphine sulfate), dihydromorphine, diacetylmorphine hydrochloride, codeine and diacetylmorphine (heroin)..." as opiate alkaloids having potent analgesic property.

The teaching of Dourish differs from the claimed invention in the specific dosage formulations (required in the claims 15-18); the specific dosage amounts of devazepide and/or the opiate (required in the claims 27-28 and 31-34); the treatment of specific side effects caused by the opiate, namely constipation, dizziness, tiredeness/fatigue and vomiting (required in the claims 35-36); the utilization of the specific enantiomer of devazepide (required in the claims 37-38); and the utilization of other opiate analgesic, namely 1,4 hydroxymorphinan opioid (required in the claims 44 and 46).

With respect to the determination of the specific delivery dosage formulations or the specific dosage amounts of devazepide and/or the opiate, such determination of delivery dosage forms or dosage amounts having optimum therapeutic index is considered well within the skill of

the artisan, and the artisan would be motivated to determine optimum dosage amounts or delivery dosage forms to maximize the therapeutic effects of the drug.

With respect to the treatment of the side effects caused by opiate such as constipation, dizziness, tiredenses/fatigue and vomiting, one having ordinary skill in the art would have been motivated to use devazepide as adjuvant to morphine analgesia allowing lower doses of the opiate to be used to relieve pain while minimizing the common adverse effects of opioid (i.e., constipation, nausea and emesis) by reducing the dosage amounts of opiate administered to the patient requiring analgesia.

With respect to the utilization of the specific enantiomer of devazepide, the individual isomers are obvious variants over the corresponding racemate because of their presence in the racemate. It would further be expected that one of the isomers would be more active than the other, and the skill artisan would be motivated to determine optimum amounts of the isomers to maximize the effectiveness of the drug.

With respect to the utilization of the 1,4 hydroxymorphinan opioid (e.g., butorphanol, codeine, dihydrocdeine, etc...), one having ordinary skill in the art would have expected that 1,4 hydroxymorphinan opioid would have similar activity as morphine, and would be motivated to use devazepide in combination with the 1,4 hydroxymorphinan opioid to potentiate the analgesic effect of the 1,4 hydroxymorphinan opioid while minimizing the side effects of the opioid by lowering the dose of the opioid to be used to relieve pain.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1-46 are provisionally rejected under the judicially created doctrine of double patenting over claims 42-58 and 97 of U. S. Patent Application No. 10/108,659.

Although the conflicting claims are not identical, they are not patentably distinct from each other because both of the instant application and the copending applications are drawn to a method of treating adverse effects of opioid with separate, simultaneous or sequential administration of a therapeutically effective amount of devazepide and an opioid analgesic to a patient requiring analgesic. In addition, the determination of therapeutic dosages and delivery dosage formulations would be considered well within the purview of the skilled artisan.

Conclusion

8. No Claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (571) 272-0951. The fax number for this Group is (703) 872-9306.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Brian Kwon
Patent Examiner
AU 1614